GenSight BIOLOGICS

Corporate Presentation

October 2023

A LEADING Gene Therapy BIOTECHNOLOGY COMPANY

GENSIGHT-BIOLOGICS.COM

Disclaimer

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Investment Case – Last Mile to LUMEVOQ® Approval

1	**Late-stage Biotech company**	Public company founded in 2012 dedicated to developing and commercializing gene therapies for neurodegenerative retinal diseases and diseases of the central nervous system. Euronext Paris Listed SIGHT
2	**Seasoned management team / Solid investor base**	Management team with strong and highly relevant Biotech experience in R&D and commercialization Solid investor base of Healthcare specialist investors, including EU and US based investors.
3	**LUMEVOQ® Strong clinical data in LHON**	LUMEVOQ® completed 3 Phase III studies in Leber Hereditary Optic Neuropathy (ND4 LHON), a rare and highly debilitating genetic ophthalmic disease leading to sudden loss of central vision and affecting c. 1,200 – 1,500 new patients / year in Europe and the US. Overall design of new Phase III RECOVER endorsed by EMA.
4	**LUMEVOQ® Defining registration pathway**	Available in France through paid Early Access at €700,000 for a bilateral injection (currently paused pending product availability in Q1 2024). Manufacturing issues successfully remediated. Ongoing discussion with EMA, UK MHRA and US FDA to confirm registration pathway
5	**Cutting edge optogenetics in Retinitis Pigmentosa**	GS030 outstanding early findings reporting blind patients to precisely identify objects (published in Nature Medicine in May 21) ; 1-yr data from PIONEER Phase I/II Clinical Trial reported in Feb 2023 Extension cohort currently being recruited, expected to be completed by year end 2023

GenSight BIOLOGICS

Seasoned Executive Team

Bernard Gilly
Chief Executive Officer

PIXIUM VISION (Since 2011)
FOVEA PHARMA (2005-2009)
SOFINNOVA PARTNERS (2000-2005)
TRANSGENE (1992-2000)

Ph.D. in biology and bio-economics

Thomas Gidoin
Chief Financial Officer

DBV TECHNOLOGIES (2012-2015)
IPSEN (2008-2011)
ERNST & YOUNG (2007-2008)

Magali Taiel
Chief Medical Officer

ProQR THERAPEUTICS (2016-2018)
ELI LILLY (2004-2016)
PFIZER (2001-2004)
SERVIER (1999-2001)

M.D., Board-certified ophthalmologist

Scott Jeffers
Chief Technical Officer

REDPIN THERAPEUTICS (2021-2022)
UNIQURE (2019-2021)
SELECTA BIOSCIENCES (2018-2019)
BRAMMER BIO (2015-2018)

Ph.D. in virology

Philippe Motté
SVP, Regulatory & Quality

GENFIT (2020-2022)
MEDDAY (2019-2020)
ABBVIE (2013-2018)
IPSEN (2004-2013)
ROCHE (1998-2004)
GSK (1991-1998)
SANOFI (1989-1991)

Pharm.D. & Ph.D. in human biology

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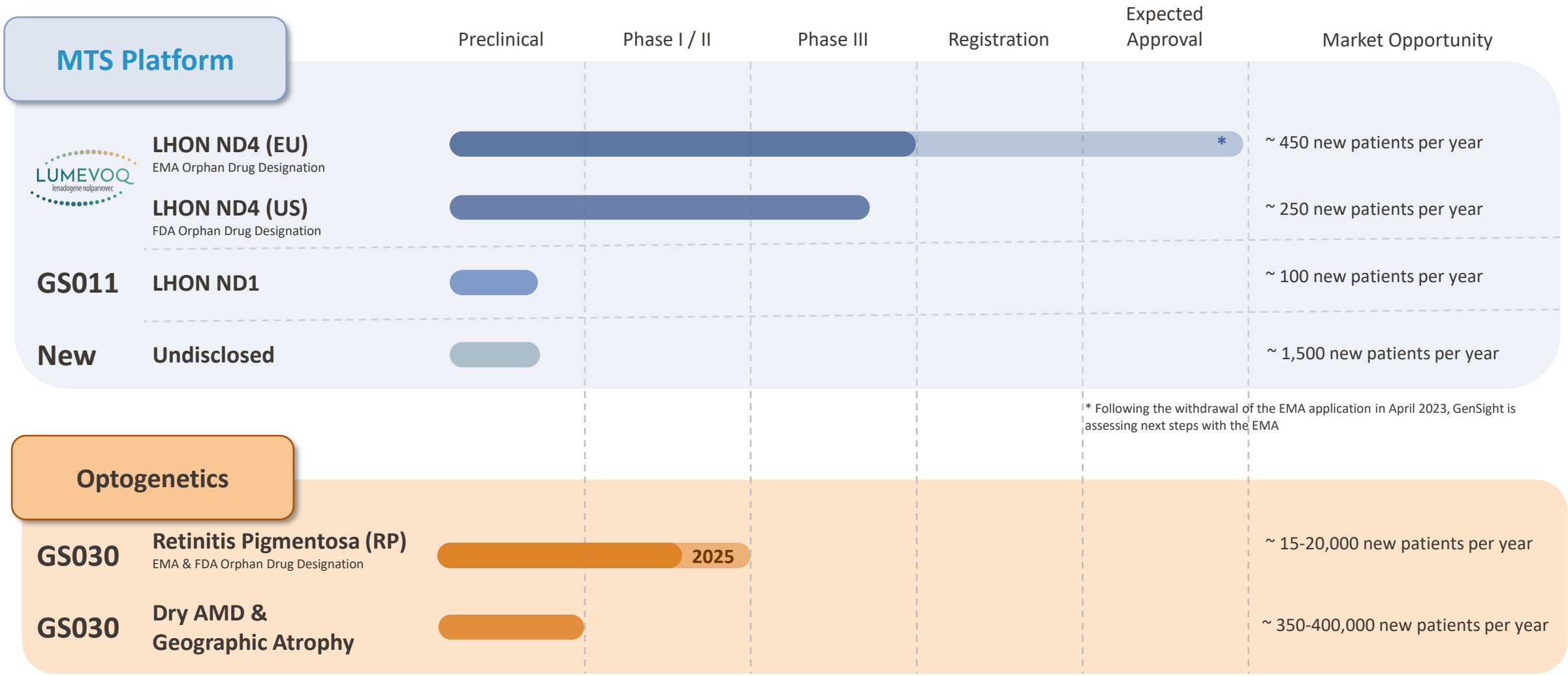
Pipeline: solid and advanced product portfolio in ophthalmic Gene Therapy



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LUMEVOQ® in LHON-*ND4*

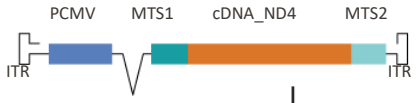
- 3 Phase III completed; additional Phase III to be initiated in Q2 2024
- New European regulatory submission planned in Leber Hereditary Optic Neuropathy

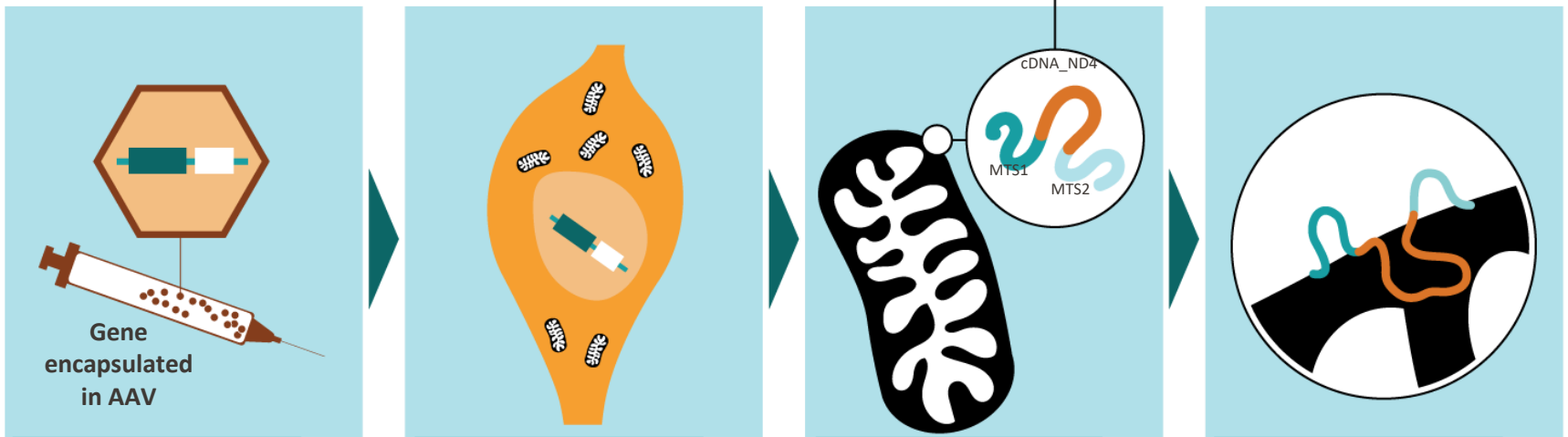
LUMEVOQ® introduces Gene Therapy solution for mitochondrial diseases

Replacing affected mitochondrial mRNA via proprietary *MTS* technology*

The product of research collaboration with Inserm

MTS in action for GS010:





Step 1

Retinal cell transduced with vector containing wild-type mitochondrial gene

Step 2

Wild-type mitochondrial gene transcribed in the nucleus

Step 3

Wild-type mRNA **delivered by MTS directly** to polysomes located at the mitochondrial surface, where protein synthesis occurs

Step 4

Finally, the wild-type mitochondrial protein is translocated inside the mitochondrion, where it **restores energy production**

Gene Therapy

*MTS**

*MTS = mitochondrial targeting sequence

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ND4 LHON: blinding bilateral mitochondrial disease

Devastating impact

- **Major cause of blindness in young adults**

Incidence	0.15/100,000
Prevalence	1/31k-40k
Blindness	15-35y

- **Causal mutation is important**

  ND4: the most severe mutation with poor visual prognosis

Acute, rapidly progressing and irreversible

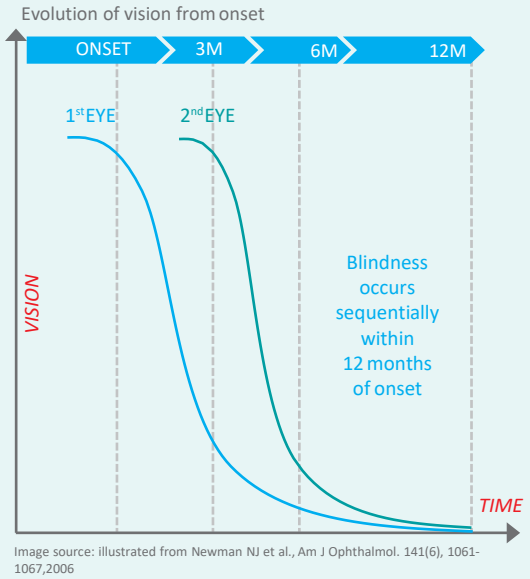

Image source: illustrated from Newman NJ et al., Am J Ophthalmol. 141(6), 1061-1067,2006

"The evolution of natural history eyes shows an absence of recovery"

Valerio Carelli et al. Indirect Comparison of Lenadogene Nolparvovec Gene Therapy Versus Natural History in Patients with Leber Hereditary Optic Neuropathy Carrying the m.11778G>A MT-ND4 Mutation. Ophthalmol Ther. https://doi.org/10.1007/s40123-022-00611-x

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Clinically meaningful and persistent visual function improvement across 3 Phase III studies

REFLECT BILATERAL

98 patients
with vision loss ≤ 1 year

Change from NADIR* in ETDRS letter equivalents	At 3 years	
	1st eye	2nd eye
2 LUMEVOQ eyes	+ 20	+17
1 LUMEVOQ eye	+ 18	+14 (*placebo*)

REVERSE 6-12 MONTHS · RESTORE RESCUE-REVERSE LONG TERM FOLLOW-UP

37 patients
with vision loss 6 ≤ 12 months

Change from NADIR* in ETDRS letter equivalents	At 5 years
	Mean
LUMEVOQ eyes	+22
Contralateral eyes (Sham)	+20

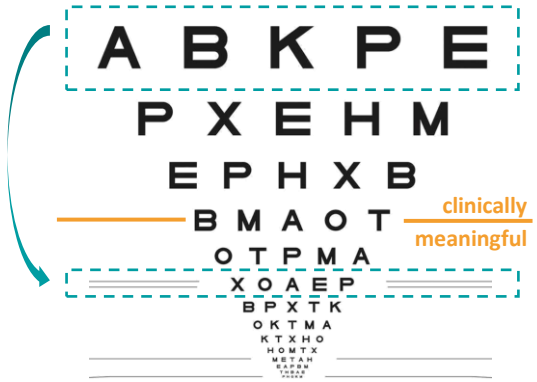
RESCUE 0-6 MONTHS · RESTORE RESCUE-REVERSE LONG TERM FOLLOW-UP

39 patients
with vision loss ≤ 6 months

Change from NADIR* in ETDRS letter equivalents	At 5 years
	Mean
LUMEVOQ eyes	+23
Contralateral eyes (Sham)	+18

Clinically meaningful improvement on **Quality-of-Life** parameters

3+ lines of visual acuity improvement vs Nadir is clinically meaningful



* NADIR defined as the **worst** **BCVA** from baseline to time point of interest (5 years for REVERSE and RESCUE, 3 years for REFLECT). Mean change from nadir: last observation for REVERSE/RESTORE and RESCUE/RESTORE (Database lock RESTORE: Jul 4, 2022, completed studies); LOCF imputation for REFLECT (data cut-off Nov 28, 2022, study ongoing). REVERSE: NCT02652780; RESCUE: NCT02652767; RESTORE: NCT03406104; REFLECT: NCT03293524.

SOURCE: GenSight data on file.

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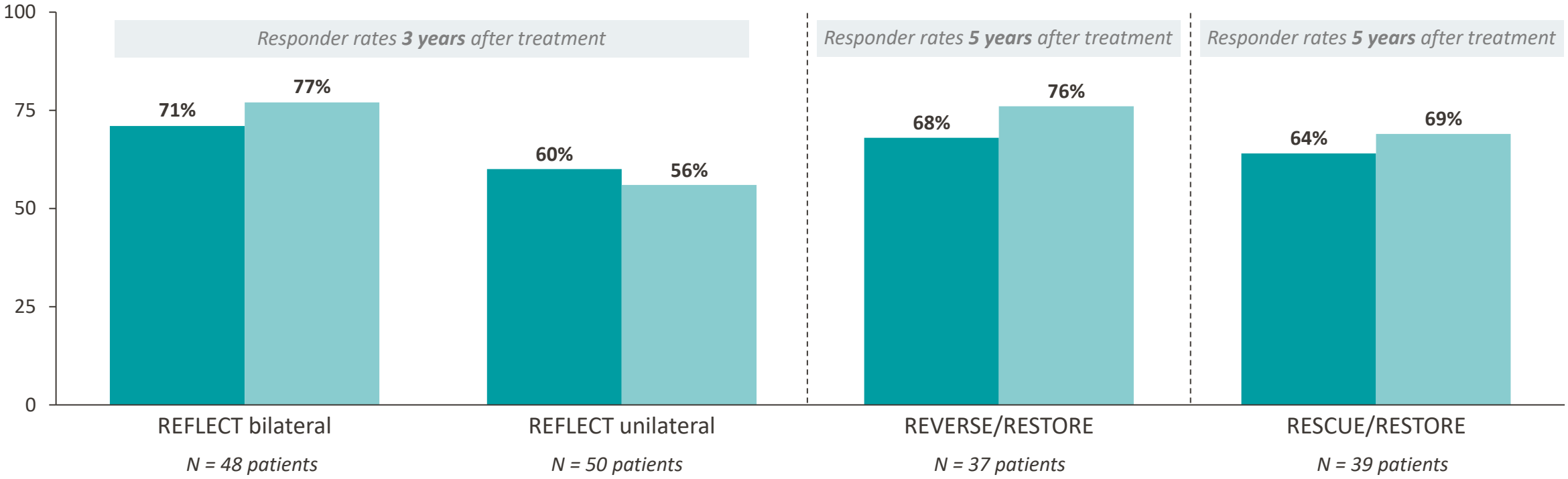
Meaningful and sustained visual function improvement for the majority of patients

Patient Responder Rates* Across LUMEVOQ® Phase III trials (%)

***Definition of "responder"**

- At least -0.3 LogMAR (+15 letters) improvement from nadir
- Clinically relevant recovery (CRR)** from nadir



Results at last observation for REFLECT (data cut-off Nov 28, 2022, study on-going)

Results at last observation for REVERSE/RESTORE and RESCUE/RESTORE (Database lock RESTORE: Jul 4, 2022, completed studies)

Notes: **CRR: on-chart BCVA gain of at least 10 ETDRS letters, or conversion from off-chart to on-chart BCVA. Patient response: best outcome observed in either eye.
REVERSE: NCT02652780; RESCUE: NCT02652767; RESTORE: NCT03406104; REFLECT: NCT03293524.

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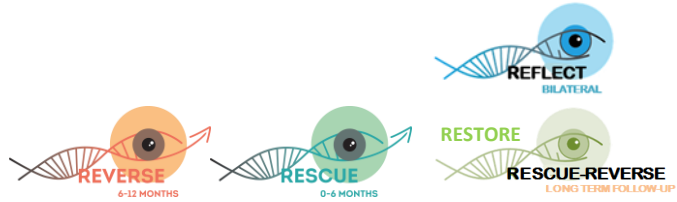
Indirect comparison to assess LUMEVOQ® treatment effect



Contralateral effect eliminated the **control group** formed by the set of eyes treated with sham/placebo injection

→Indirect comparison of Lumevoq data versus an **external** control group to assess efficacy of the gene therapy

Treated Group
174 ND4 LHON patients / 152 eyes

3 Phase III studies with long term follow-up[1]

- REVERSE/RESCUE/RESTORE: 76 patients
- REFLECT: 98 patients
- Sham and placebo eyes included in the treated group, in line with the contralateral effect

Untreated Group (External Control)
208 patients / 408 eyes

11 Natural History studies[2]

Composed of patients with same demographics as treated group
- *ND4* mutation, age ≥15 years old
- BCVA adjusted on time from vision loss

- Individual Patients data
  - enabling robust indirect comparison methodology

[1] REVERSE: NCT02652780; RESCUE: NCT02652767; RESTORE: NCT03406104; REFLECT: NCT03293524
[2] Eleven NH studies: Yu-Wai-Man 2021, Lam 2014, Yang 2016, Romero 2014, Zhou 2010, Qu 2009, Qu 2007, Sadun 2004, Hotta 1995, Nakamura 1993, Newman 1991.

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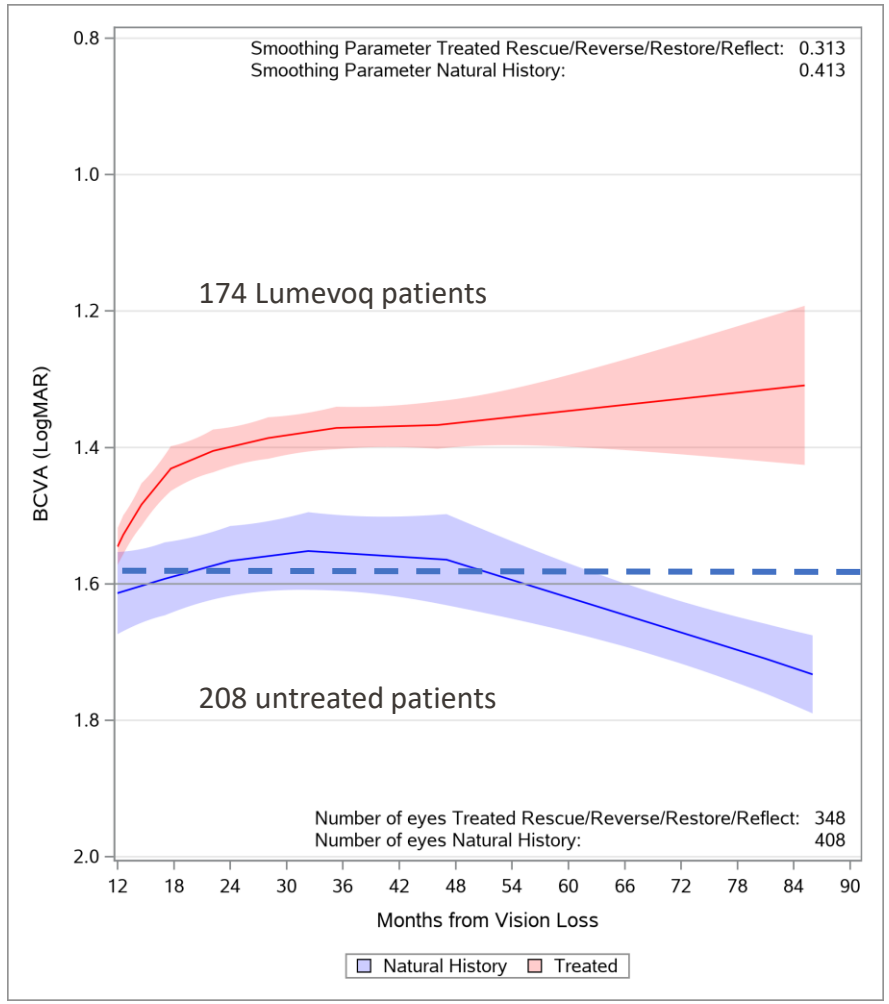
Visual improvement after LUMEVOQ® treatment contrasts sharply with natural history

Clinically significant improvement of visual acuity persistent over time for Lumevoq® efficacy pool versus Natural History



BCVA : best corrected visual acuity. SOURCE: GenSight data on file.

- Evidence of efficacy drawn from **three Phase III trials – unprecedented** for a rare disease drug

REVERSE: NCT02652780; RESCUE: NCT02652767; RESTORE: NCT03406104; REFLECT: NCT03293524

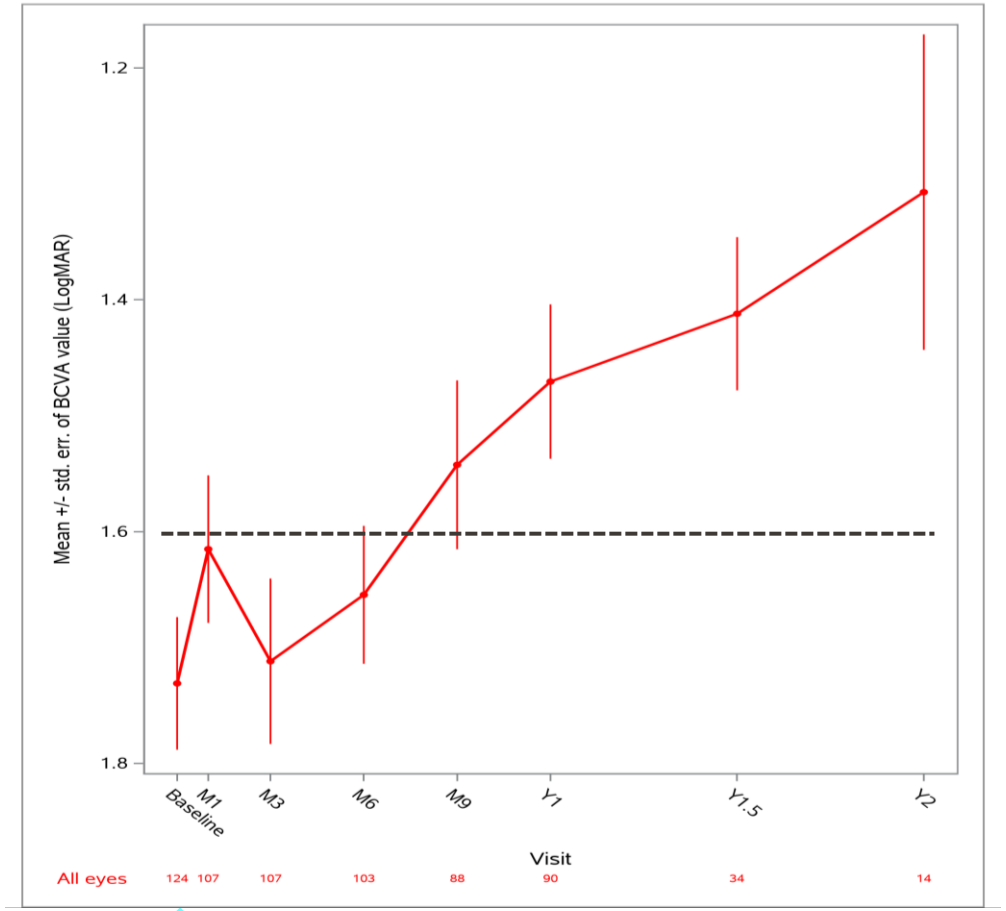
- **Sustained improvement:** Evolution of visual function **statistically better** than in historical cohort and with **clinical relevance**

- The **magnitude** of the difference of effect in LUMEVOQ®-treated patients compared to natural history patients is **unlikely to be solely attributed to residual biases** related to the indirect comparison methodology. The effect observed in LUMEVOQ®-treated patients **could not be explained by spontaneous improvement**.

Notes:
- Models used individual *ND4* patient data.
- LOESS regression (solid lines) with 95% CI around the fitted curves (shaded areas) of BCVA values up to 86 months (values >86 months were assigned to the 86-month timepoint [reverse LOCF]).
- Smoothing parameter: 0.313 for treated eyes and 0.413 for NH eyes.
- Treated patients received a single unilateral or bilateral injection of Lumevoq® between 0 and M12.
- Curves start at M12 as nearly all eyes (96.8%) had been treated at M12.

Prospective data from early access programs (EAP) confirm results of LUMEVOQ® trials

Evolution of mean visual acuity over time (n=63)



Datacut off: March 2, 2023

LUMEVOQ® treatment
Mean (SD): 11.30 (9.66) months
post Vision Loss

Treated patients under EAP (n=63)
Results at last observation

Last Observation = time post-treatment (in months)	*Mean (SD): **13.37** (5.94)* *Median: **12.16***
Mean change in visual acuity (vs. nadir)	-0.43 LogMAR = **+21.5 letters ETDRS**
% of eyes with on-chart vision	**63.5%**
Clinically relevant recovery (CRR) from nadir at eye level (%)	**52.4%**

SD: Standard Deviation

SOURCE: NANOS 2023 – Abstract - Use of Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy in Early Access Programs. Catherine Vignal-Clermont et al.

Favorable safety and tolerability profile

- **No study discontinuations** related to treatment or study procedure[1]
- **Excellent systemic tolerance**, related to the **limited biodissemination**[2]
- **Mostly mild** intraocular inflammation[3], which was **responsive to conventional treatment**[4], mostly corticosteroid eye drops alone

> **REVERSE and RESCUE**: No prevention of intraocular inflammation: no requirement for oral corticosteroids
>
> **REFLECT**: Per protocol, for prevention of intraocular inflammation: Oral corticosteroids: 40 mg for 2 days before administration of the gene therapy, 40 mg for the first week after administration, 30 mg for the second week, 20 mg for the third week, and 10 mg for the fourth week.

- **Comparable favourable safety profile for unilateral and bilateral** administration

Notes:
1. No study discontinuation due to ocular adverse events (AEs); no ocular serious AEs (SAEs) in treated eyes (only 1 ocular SAE in a sham eye: retinal tear, unlikely related to treatment/procedure)
2. Negligible in the blood, not detected in the urine and limited and of short duration in the tears
3. The intraocular inflammation was considered likely to be related to the drug and occurred in the anterior chamber and the vitreous.

SOURCE: Safety of Lenadogene Nolparvovec Gene Therapy Over 5 Years in 189 Patients With Leber Hereditary Optic Neuropathy. Catherine Vignal-Clermont et al. AJO 2022. https://doi.org/10.1016/j.ajo.2022.11.026
REVERSE: NCT02652780; RESCUE: NCT02652767; RESTORE: NCT03406104; REFLECT: NCT03293524.

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Regulatory path forward for LUMEVOQ®

- Defining the next steps for a new MAA
- Scientific advice received and further interactions planned

- Interactions (scientific advice) ongoing to explore a UK-MA regulatory path

- Phase 3 trial design discussions ongoing

- Supply for Early Access program "*Autorisation d'Accès Compassionnel/Précoce*" or AAC/AAP (former ATU) granted by ANSM expected to restart by Q1 2024
  - *"ATU Nominative* or ATUn*"* - named patient Temporary Authorization for Use - for LUMEVOQ® first authorized by ANSM to CHNO of the *Quinze-Vingts* in Paris in December 2019

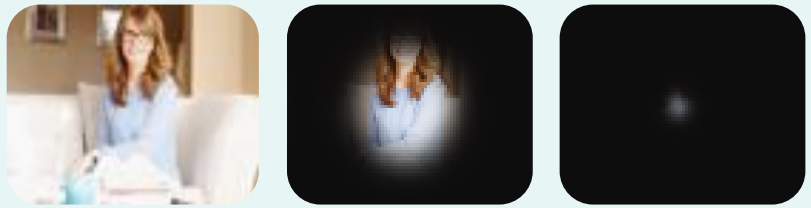
GS030

Second product candidate targeting photoreceptor degenerative diseases:

- Retinitis Pigmentosa (RP)
- Age-Related Macular Degeneration (AMD)

Treating the 2 main degenerative diseases of photoreceptors that lead to blindness

Retinitis Pigmentosa (RP)



- Blinding genetic disease
- Mutations in over 100 different genes
- Photoreceptor degeneration leads to slow & irreversible progression to blindness, usually at age 40-45
- 15-20,000 new patients each year in the US and EU

Geographic Atrophy (GA) in AMD (Age-Related Macular Degeneration)

- Early (dry-form) AMD evolves with age into late AMD, one of whose forms is GA
- Dry-AMD affects 350-400,000 new patients a year
- Prevalence of GA increases with age, from 3.5% among 75-year-olds to 22% among those over 90
- Late AMD patients with GA account for 10-20% of blind patients in their age group

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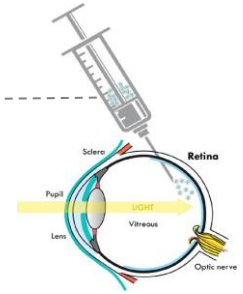
GS030 Optogenetic Therapy : Combining Gene Therapy and Medical Device

Drug Product

GS030-DP

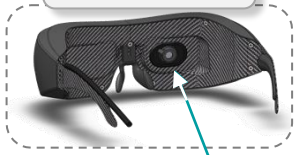
ChrimsonR gene

AAV2.7m8 vector

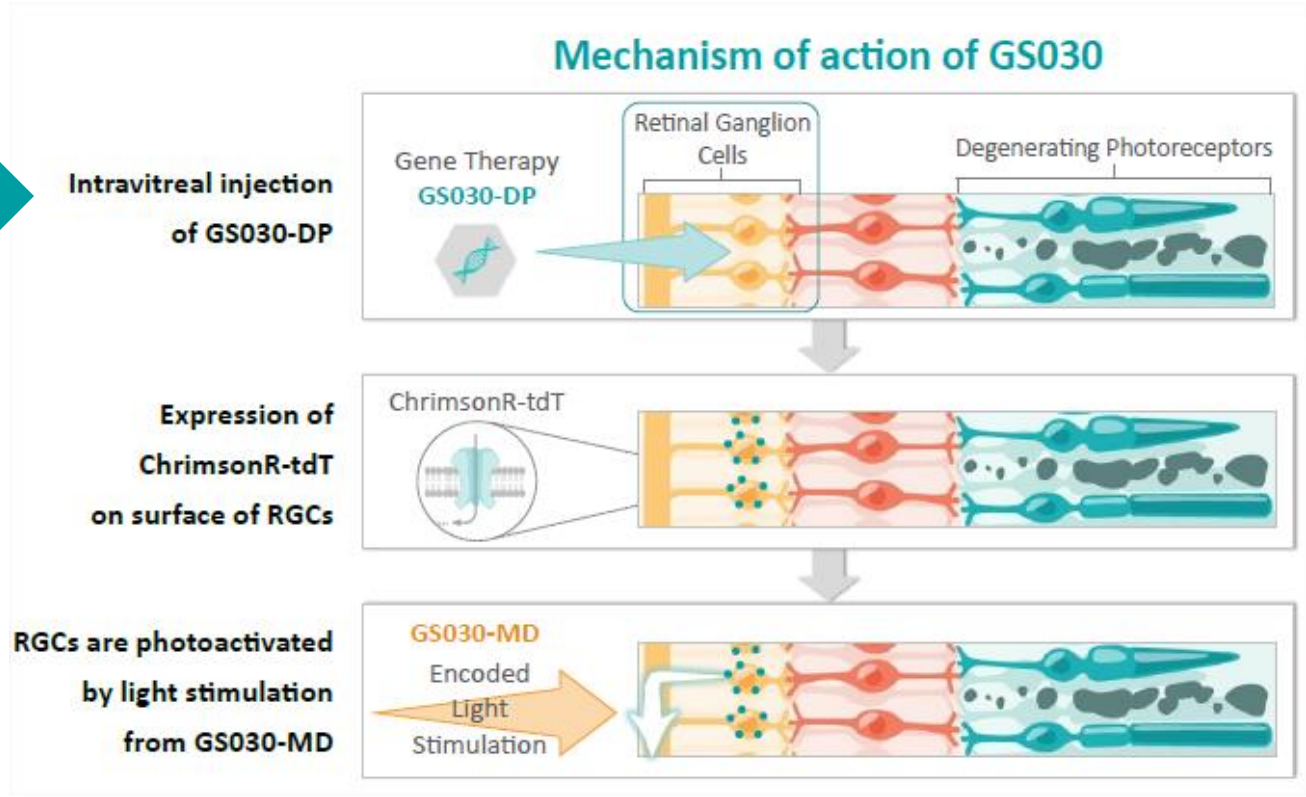


Medical Device

GS030-MD



Light Projector



- **Restore light sensitivity to diseased retina, independently of causative mutation**

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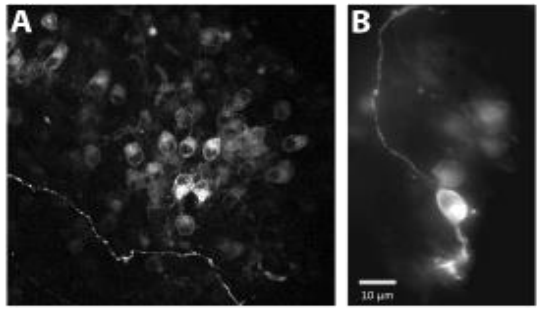
GS030 leads to functional vision restoration in monkey and rats

Localization of light-sensitive protein in NHP retina

Expression of ChrR-tdT in midget cells of monkey perifovea

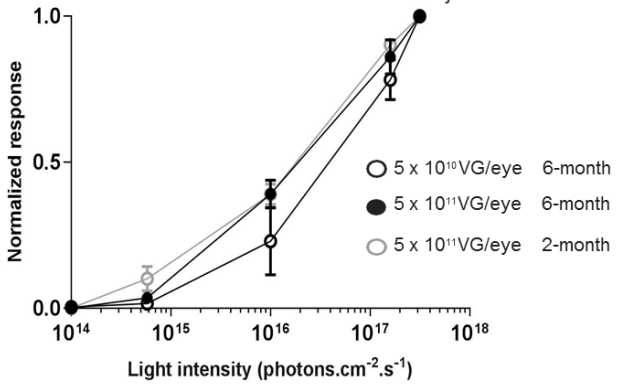
In vivo in NHP assessment 6 months after IVT injection



Dose-ranging response to firing relationship in NHP

Active dose range : 5x10^{10} and 5x10^{11} VG/eye

MEA assessment 6 months after IVT injection in NHP



Recent publication

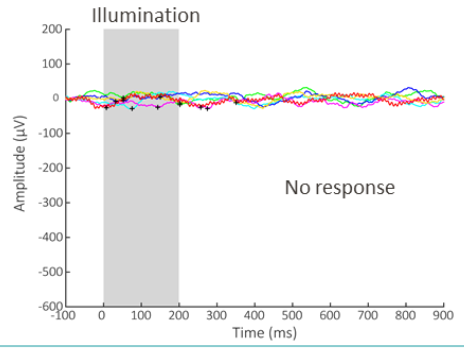
Optogenetic therapy: high spatiotemporal resolution and pattern discrimination compatible with vision restoration in non-human primates. Gauvain G. et al. **Communications Biology, Feb. 2021**
https://www.nature.com/articles/s42003-020-01594-w.

Restoration of a functional vision in P23H rats

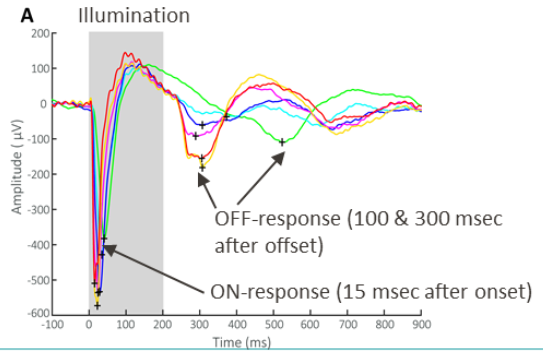
Light-induced visual evoked cortical responses

Full field 590 nm light from ~ 4.7x10^{15} to 1.1x10^{17} photons/cm^2/sec

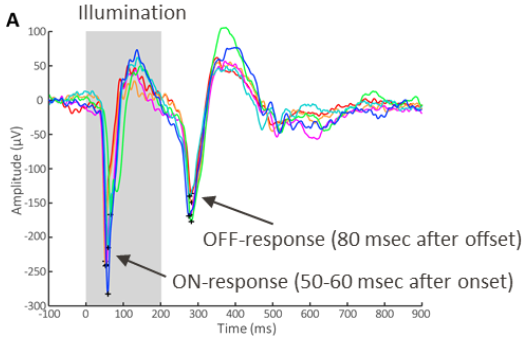
Untreated P23H rat



GS030-treated P23H rat



Normal Long-Evans rat



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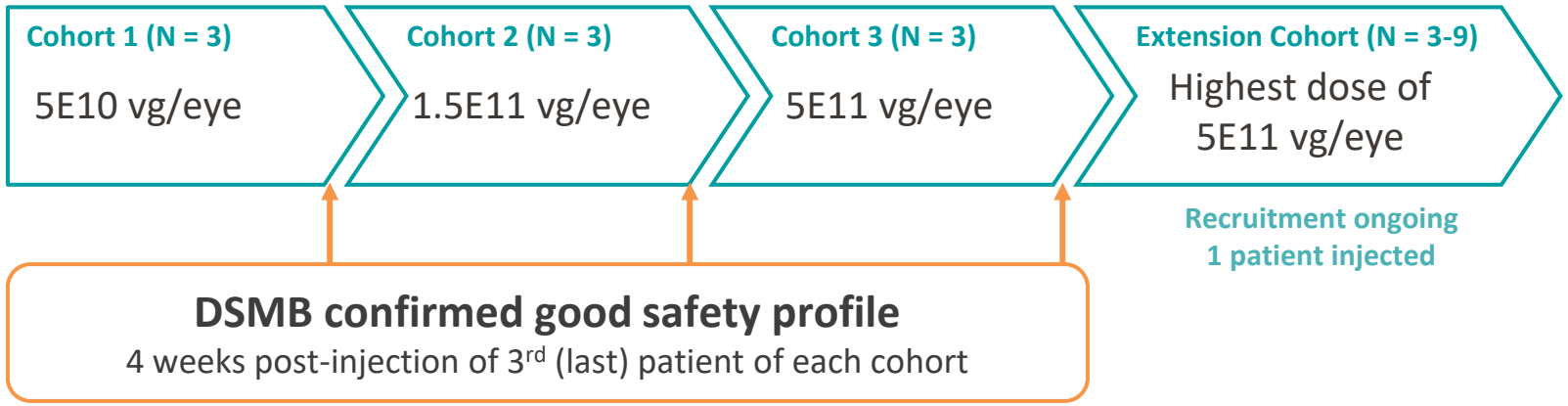
PIONEER Phase I/II clinical trial: In late-stage Retinitis Pigmentosa

Study design



- **Phase I/II**, dose-escalation safety study, multi-center (France, UK, US)
- **Study population:** end-stage non-syndromic RP (vision ≤ Counting Fingers)
- Single intra-vitreal injection in the **worst affected** eye
- Decision to increase the dose taken by a DSMB
- **Primary analysis:** Safety at 1 year
- Follow-up of 5 years

Dr Elise Boulanger-Scemama Dr Isabelle Audo	**CHNO Les Quinze Vingts**	**France**
Dr Joseph Martel	**UPMC Eye Center**	**USA**
Dr Simona Degli Esposti	**Moorfields Eye Hospital NHS Foundation Trust**	**UK**
Dr João Pedro Marques	**CORC (Coimbra Ophthalmology Reading Center)**	**Portugal**

Extension Cohort recruiting with highest dose 5E11 vg/eye without any modification after DSMB#3 recommendation

PIONEER Phase I/II clinical trial: A favorable safety and tolerability profile

- **No study discontinuations** related to treatment or study procedure
- **Excellent systemic tolerance**, related to the **limited biodissemination**
- **Mostly mild** intraocular inflammation, which was **responsive to conventional treatment**, mostly corticosteroid eye drops alone
  - No increased severity at high dose

> Per protocol, for prevention of intraocular inflammation: Oral corticosteroids: 0.5 mg/kg for 1 week before administration of the gene therapy, 1 mg/kg for the first week after administration, 0.5 mg/kg for the second week, 0.25 mg/kg for the third week, and 0.125 mg/kg for the fourth week.

- **Light stimulating googles well-tolerated**

Notes:
1. The intraocular inflammation was considered likely to be related to the gene therapy and occurred in the anterior chamber and the vitreous..

SOURCE: GenSight data on file; Sahel JA et al, (PO332) Optogenetics in the Clinic: Safety and Efficacy Updates on the Phase Clinical Trial PIONEER, abstract presented at AAO 2022

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PIONEER Phase I/II clinical trial: Encouraging signs of efficacy in the highest dose cohort

Efficacy signal at one year

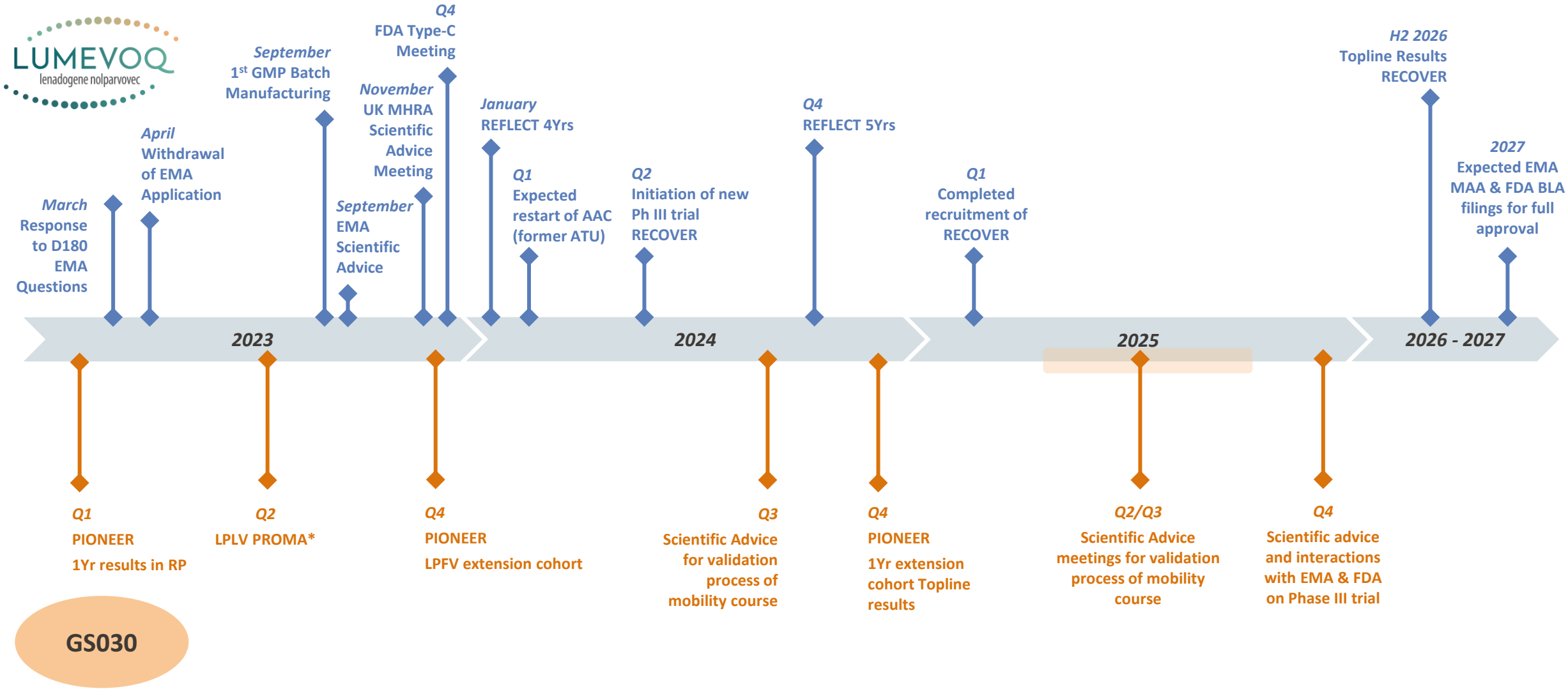
- Released in Feb 2023, when the patients from the highest dose cohort have reached 1-year post gene therapy treatment
- Encouraging signals of efficacy at one year post treatment:
  - Some patients had their vision improved from being barely able to perceive light before treatment to being able to locate and count objects at one year post treatment
  - Best results at the highest dose

Results at one year released in Feb 2023

GenSight Biologics Announces 1 Year Safety data and Efficacy signals from PIONEER Phase I/II Clinical Trial of GS030, an Optogenetic Treatment Candidate for Retinitis Pigmentosa

Corporate & Finance

Rich upcoming news flow with numerous inflection points



*Development of mobility course, started in 2021; PROMA study: *PROtocole de Mobilité Adapté pour des sujets Déficients Visuels Avancés*: Study for validation of mobility course. Supported by GenSight for use PROMA mobility course as primary endpoint in Phase III study

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GenSight Biologics in numbers

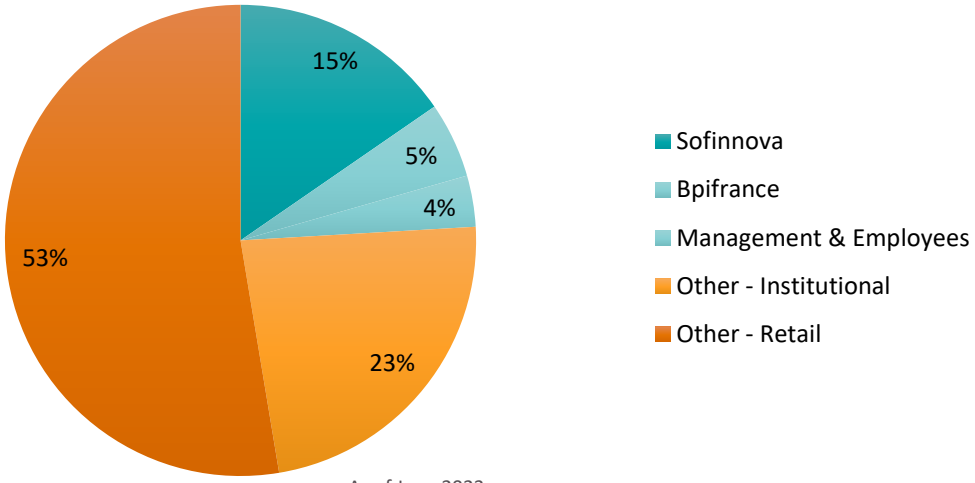
Key financial information

Company Overview	
Market Cap* :	€ 33m
Cash Position : (June 30, 2023)	€ 1.0m + €10m *(financing announced on Aug 3)*
Outstanding Shares:	46.3m
Latest Equity Raised : (March 2021)	€ 30m
Equity raised to date	€ 197m
IPO Date	July 13, 2016

*As of October 2, 2023

Analyst Coverage	
CHARDAN	Daniil Gataulin (US)
BRYAN, GARNIER & CO	Alex Cogut (FR)
ODDO BHF	Damien Choplain (FR)
Kepler Cheuvreux	Justine Telliez (FR)
Degroof Petercam	David Seynnaeve (BE)
BioMed Impact	Lionel Labourdette (FR)

Shareholder structure



As of June 2023

Corporate calendar	Date
2023 3Q Cash Position	**October 26, 2023**
2023 4Q Cash Position	January 25, 2024

GenSight BIOLOGICS

GenSight Biologics: Take Away

- Late-stage biotech with **revolutionary solutions** fulfilling the promise of **gene therapy** and **optogenetics**
- **Seasoned management team** and **solid investor base** to back up the focused portfolio
- **LUMEVOQ®** for Leber Hereditary Optic Neuropathy
  - Significant and sustained **visual function improvement** for the majority of patients, contrasting with **absence of recovery in natural history**
  - CMC challenges successfully remediated
  - Drive to align with regulatory authorities' expectations, including endorsement for overall design of new Phase III trial from European authorities
- **GS030** as **mutation-agnostic**, optogenetic treatment for Retinitis Pigmentosa
  - **Efficacy signals** in ongoing Phase I/II trial
  - Potential application to **other diseases** that damage photoreceptors
- **End of October 2023 runway, to be extended to December 2023** with the pending drawdown of August €10m Bridge 2nd Tranche (€4m). **GenSight will seek additional equity funding in Q4 2023** to extend its cash runway into 2024.